GIANT CELL TUMORS NOT CONNECTED WITH BONES

By LENORE D. CAMPBELL *

Since the one constant and outstanding feature is the presence of giant cells, and since the real nature is undetermined, the simple term "giant cell tumor" of tendons, etc., might be employed in this class of growths. The descriptive adjective "xanthic" could be used when "foam cells" and yellow color are found. The term "sarcoma" is misleading and should not be used.

Since their benign character has been established, amputation is to be avoided and local conservative treatment advised.

It would be well for all work on these cases to be reported that the exact nature and origin be more accurately determined.

DISCUSSION *by Roy W. Hammack, Los Angeles; G. Y. Rusk, San Francisco.*

THE purpose of this paper is to review the pathology of this comparatively rare condition, and to report three new cases.

The literature dealing with the subject, particularly with reference to giant cell tumors of the extremities, is voluminous.

The first nonosseous myeloid tumor was recorded by Broca in 1860. Four new cases were reported during the next twenty-five years, and the number rapidly increased until in 1913 Tourneux collected fifty-four examples. Stewart and Flint in 1915 found seventeen additional cases and reported two from Leeds, bringing the total up to seventy-three. Of these, two-thirds had been published by French and German authors. Broders in 1919 reported seventeen others from the Mayo clinic. Garrett in 1924 collected thirty fibromas in tendon sheaths from Johns Hopkins, the first occurring in 1896. These, with a few others reported during the last five years, brings the total number to about 130.

There are varied opinions concerning the real nature of the growth. All of the early observers called them giant cell sarcomas. Heurteux in 1891 did the first careful study and divided them into two groups: those more embryonic and rapidly growing, and those with more adult characteristics and slower growth. Certain French observers classed them under the general name "myelome," including those of osseous and those of fibrous origin.

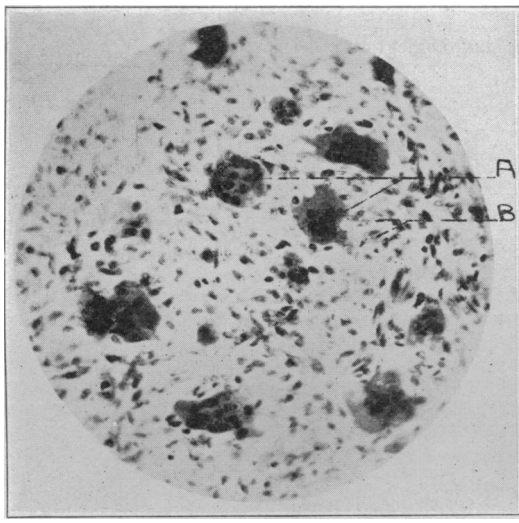
Dor in 1898 was the first to describe the presence of xanthoma cells, and suggested the name "myeloxanthoma." Bonjour in 1897 thought they should be in a group falling between the sarcomas and fibromas. Bonhomme in the same year regarded the growth simply as a chronic inflammatory process. Targett considered these giant cell tumors malignant. Bellamy in 1901 made a detailed study of four cases and called them myeloid endotheliomas, as did also Grant and Stewart in 1914. Tourneux believed they were sarcomas of low malignancy, and classed them as xanthic tumors with giant cells. Flessig in 1913 advanced the theory that they were granulomatous in nature, noting their resemblance to granulation tissue, the presence of xanthoma cells, and deposits of crystalline cholesterin associated with the giant cells in one case. He suggests the name of granuloma of tendon sheaths. Dunn thought they were on the border line between tumor growths and granulomas. Broders used the noncommittal descriptive term "benign xanthic extraperiosteal tumors of the extremities containing foreign body giant cells." Ewing discusses them under giant cell sarcomas. Buxton in 1922 called his two cases giant cell myelomas. Garrett in 1924 discusses his under the general head of xanthoma, and the subheading, fibroma of tendon sheaths; referring to Bloodgood's paper in 1905 in which the same term was used. He suggests we might call them endothelio-granulomas. Den Hartog in 1924 reports two cases from Amsterdam under the title, "So-called Xantho-Sarcomas."

So we see all opinions have been held from that of true sarcomas to simple granulation tissue, and the vocabulary has been nearly exhausted for a suitable descriptive term. Although the exact name is unsettled, the pathology is quite definite, as well as the clinical fact that they are essentially benign and should not be classed as sarcomas.

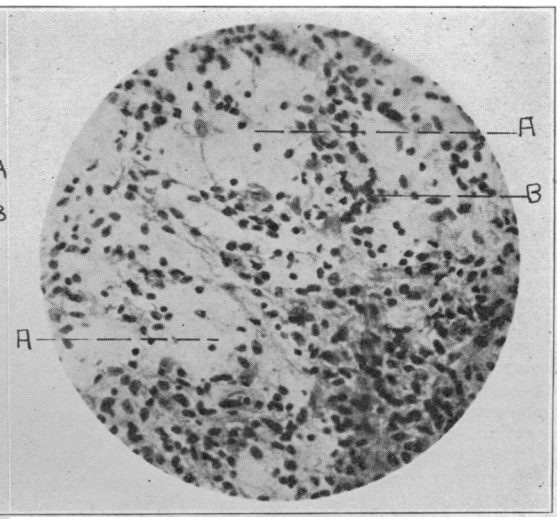
I shall briefly summarize the clinical picture and pathology as described by others. Etiology: In one-third of the larger series there is a history of trauma or of local inflammation. Age and sex: The sexes are affected in equal numbers. No age is exempt, but they are most frequent between 10 and 20 years. Symptoms: The only complaint is of a localized swelling, usually causing no interference with function. Location: They are found principally on the tendon sheaths or aponeuroses of the hands and feet, and most frequently on the flexor tendons of the right hand (where exposed to excessive friction). They are usually single, although a few have been multiple, and one case of bilateral growths on the tendon Achilles was reported by Ollerenshaw. They are small in size and not adherent to the bone. Duration: They are of slow growth, reaching moderate dimensions after a period of one to twenty years. Malignancy: All agree they are benign when below the elbow or the knees, and possibly malignant when above. They never form metastases and rarely recur, although 15 per cent of recurrences were reported by Garrett, which were cured by a second removal. Treatment: Amputation is unnecessary and local excision is all that is required. Macroscopic appearance: The tumors are small in size, seldom reaching the size of an egg, and are hemispherical or bean-shaped. They are firm, encapsulated, gray to yellowish pink in color, and often mottled by brown patches. Cut surface shows white streaks of fibrous tissue and marked lobulation. Microscopic appearance: This presents four main features, viz.: (*a*) stroma; (*b*) cellular elements; (*c*) vessels; (*d*) degenerative changes.

(*a*) Stroma: A dense fibrous capsule surrounds the growth and trabeculae extend inward, forming a supporting stroma and dividing the tumor into lobules. This shows some fibroblasts, is frequently infiltrated with tumor cells, and shows hyalinization

* **Lenore D. Campbell** (Loma Linda, California). M. D. College of Medical Evangelists, Loma Linda. Practice limited to Pathology. Hospital connections: Loma Linda Sanitarium and Hospital; White Memorial Hospital, Los Angeles; San Bernardino County General Hospital.



Illus. 1—Photomicrograph of tumor in Case 3.
A—Giant cells.
B—Tumor cells.



Illus. 2—Photomicrograph of tumor in Case 2.
A—Xanthoma or "foam" cells.
B—Tumor cells.

and pigment deposits. (*b*) Cellular elements: The mass of the tumor is made up of groups of round or polyhedral cells about 12 microns in diameter, with vesicular nuclei and distinct nucleoli. Few mitotic figures are seen. Giant cells of foreign body type are found in typical cases. They range from 9 to 100 microns in size, contain from 2 to 100 nuclei grouped centrally, and are scattered throughout the tumor. In over half the cases, xanthoma or "foam cells" are present. Broders found them in 64 per cent. These are round cells having a distinct cell membrane, a small dark nucleus, and very pale, staining cytoplasm which is filled with cholesterin lipoid material. They are located in groups principally at the periphery of the growth, and give it the yellow color, hence the term "xanthic."

Wandering cells, mononuclears chiefly, are occasionally seen, but are not prominent. (*c*) Blood-vessels: These are abundant and frequently show signs of endothelial proliferation. Thin-walled, incompletely lined spaces are also described. (*d*) Degenerative changes are always present. Crystalline cholesterin deposits in the tissue spaces are noted in some instances, and the lipoid material in foam cells is thought to be due to a degenerative change by some. Stewart and Flint examined frozen sections by the polarizing microscope in one of their cases, and proved a complete lack of doubly refracting lipoid. Cholesterin, then, is not constantly present and probably has no etiological significance.

Hemorrhage and hematogenous pigment causes the brown patches seen grossly. The pigment deposits are composed of hemosiderin, and give a Prussian-blue reaction. It is believed to be caused by trauma and repeated hemorrhages. Calcareous deposits have been observed by some.

REPORT OF CASES

Case 1—Jewish woman; age 60. Admitted to White Memorial Hospital February, 1925. Complaint: Growth on finger which began as a small nodule five months ago. No pain. No history of injury. Patient is accustomed to gardening and hard work. A small, round nodule the size of a pea was seen on the lateral surface of the left ring finger near terminal phalanx. No tenderness or ulceration. Tumor was removed, using local anesthesia. The wound healed quickly, and there has been no recurrence to date. Gross: Small, lobulated, grayish tumor 6 mm. in diameter. Microscopic: In sections the tumor is seen 2 mm. below the surface epithelium. The structure is characteristic of the types described above, showing abundant stroma, polygonal cells arranged in strands, large number of foreign body giant cells, and a deposit of yellow-brown pigment. This is a typical example of a giant cell tumor of a tendon without xanthoma cells and giving no history of injury. The clinical course and microscopic picture confirm its benign nature.

Case 2—Woman; age 60. Entered Loma Linda Sanitarium May, 1925, complaining of a small growth on the dorso-lateral surface of left index finger near terminal phalanx. This had been present for many years. It was removed under local anesthesia May 17. An irregular growth was found attached to the extensor tendon. Gross: Small oval-shaped flattened mass, 15 x 13 x 6 mm. in size. This is smooth, encapsulated, firm, and yellow in color. Cut surface appears lobulated, gray in central portion, and yellow with brown streaks at the periphery. Attached to this is some dense fibrous tissue in which two small flat tumors of similar appearance are embedded. Microscopic: Sections present typical structure of a giant cell tumor. There is a dense connective tissue capsule, and abundant hyalinized stroma. The smaller tumor cells show occasional mitotic figures. Giant cells are numerous, and many show marked eosinophilic cytoplasm. A few true tumor giant cells with vesicular overlapping nuclei are seen. Masses of pale-staining xanthoma cells are found at the periphery of the growth. Scharlach R stains them bright red. Much yellowish-brown pigment which gives a Prussian-blue reaction is noted. This is a second example of a tendon sheath tumor showing xanthoma cells and other characteristic findings. It differs from the usual in being multiple.

Case 3—Irish male; age 40. Occupation: Lumberman. Admitted to Boyle Avenue Dispensary October 3, 1924. Complaint: Swelling on right side of neck, dyspnea, husky voice, and general weakness. Symptoms began two months ago. No history of injury. A large, smooth swelling in the region of the thyroid was felt on the right side. This was firm, not tender, and slightly movable. Laryngoscopic examination showed a smooth tumor mass bulging into the larynx, obliterating the view of the right vocal cord. The left cord was thick and swollen. Clinical diagnosis: Carcinoma of larynx or thyroid. Operation was performed January 26, in which a preliminary low tracheotomy was done and the larynx opened. A tumor was found bulging into the soft tissues of the neck and into the laryngeal cavity. No connection was found with any bone. It was impossible to

remove this in one mass, so it was curetted out in pieces by the surgeon, Dr. Hayton. The right cord and ala of the thyroid cartilage were also removed. Wound healed well and the patient was last seen on May 12, after he had taken a series of deep x-ray treatments. He breathes freely and could speak in a whisper. There was a slight swelling on the right side of the neck, but no glandular enlargement. It is too soon to be certain of a cure. Gross: Specimen consists of numerous irregular masses of grayish-red tissue and several pieces of cartilage, pieces ranging in size from .5 to 1.5 cm. The cut surface shows streaks and lobulation. Microscopic: This is a very cellular growth showing varied amounts of stroma. The appearance is similar to that in Case 1. There are greater numbers of giant cells which have eosinophilic cytoplasm. Some show phagocytic activity. The blood-vessels show definite signs of endothelial proliferation. Mitotic figures are occasionally seen. There are numerous deposits of brown pigment giving the Prussian-blue reaction. Stains for neutral fat show collections of fine droplets, principally in the stroma. Scattered through the tumor are spicules of bone and masses of cartilage. This is a giant cell tumor similar to those of tendon sheaths, but originating in an unusual location. (The question of origin from bone is excluded by the location of growth and statements of surgeon.) Bony changes probably took place during its development.

SUMMARY

More than 130 cases of giant cell tumors not connected with bones have been recorded, mostly by European workers.

Various names have been applied to these growths, as xanthoma, myeloma, endothelioma, and granuloma, but none has been universally accepted.

All agree that they are benign tumors and are cured by local excision, repeated if necessary. They are most frequently located on the flexor tendons of the hands and feet, and a history of injury is obtained in about one-third of the cases.

Macroscopically, they are small, encapsulated, lobulated growths, and yellowish or pink in color. Microscopically, the characteristic features are capsule and fibrous stroma, groups of small round tumor cells, numerous foreign body giant cells, frequently xanthoma or "foam cells" and collections of hemosiderin. Two new cases of giant cell tumor of tendons are discussed.

Another incidence of giant cell tumor of similar structure is described which apparently originated in the cartilages of the larynx.

CONCLUSIONS

1. Since the one constant and outstanding feature is the presence of giant cells, and since the real nature is undetermined, the simple term "giant cell tumor" of tendons, etc., might be employed in this class of growths. The descriptive adjective "xanthic" could be used when "foam cells" and yellow color are found. The term "sarcoma" is misleading and should not be used.

2. Since their benign character has been established, amputation is to be avoided and local conservative treatment advised.

3. It would be well for all work on these cases to be reported that the exact nature and origin be more accurately determined.

DISCUSSION

ROY W. HAMMACK, M. D. (Pacific Mutual Building, Los Angeles)—Tumors of this group are not numerous and are of little clinical importance. But they may assume great importance if, as not infrequently happens, they are wrongly interpreted. The pathological diagnosis of "giant cell sarcoma" has led to unnecessary surgery. And so I believe that Doctor Campbell is entirely right in saying that these new growths should be called "giant cell tumors" or by some other innocuous term, and not sarcoma.

While it is true that in Doctor Campbell's third case the tumor was not connected with preformed bone, the structure seems more like that of the giant cell tumors of bone, and may belong to that group rather than to the group represented by the other two cases.

G. Y. RUSK, M. D. (University of California Medical School, San Francisco)—The paper presents a valuable summary of the various ideas which have developed regarding this rather unusual type of growth found in association with tendon sheaths. That this type should be considered a true neoplasm, appears from its progressive and expansive, if benign, growth. They occur in places which are subject to trauma, and hemorrhage into their substance with secondary pigmentation may readily occur; possibly the fatty substances encountered represent lipoids of red cells, which lipoids have not been removed by the sluggish circulation of the part. The giant cells appear of foreign body type, and probably represent local irritation reactions in part associated with the lipoids. That mitoses are usually seen in small numbers may have led to their classification as sarcomata, and it becomes a matter of definition where they shall be placed. Personally I prefer to use a descriptive designation analogous to what the writer proposes.

The third case presents factors differing from the other two. From the report it appears to be of the giant cell sarcoma or epulis type, and probably the prognosis is not so favorable, especially on account of the difficulties encountered during surgical removal.

DOCTOR CAMPBELL (closing)—In closing, I wish to add a brief report of two cases which have come to my attention since writing this paper. One, the case of a woman with a small tumor of the thumb, was not unusual in any way, but presented the characteristics of this type of growth. The other was a man, age 51, who complained of a large growth on the right ankle. Thirty years before, he had sustained a bad sprain here, and three years later a small nodule appeared. This gradually grew to the present size. The growth was excised, and the patient made a rapid recovery.

The tumor measures 10 x 5 x 4.5 cm. and is surrounded by a fibrous capsule. The cut surface is yellow and brown mottled, and presents gray streaks of fibrous tissue dividing it into lobules. Sections show abundant hyalinized stroma and a few foreign body cells. The tumor cells are small and arranged in rows or groups, and large numbers of pale-staining, fat-laden cells are present. Microchemical tests show that some of these cells contain both lipoid material and iron pigment. Some show a reddish color with Nile Blue sulphate and appear crystalline. This case is rather interesting, in that it is (to my knowledge) the largest growth of its kind reported, the largest in Broder's series being 8.7 cm. It is also unusual in the great predominance of lipoid-containing cells.

I wish to thank Doctors Hammack and Rusk for their discussions.

Before you start to interfere with your present bodily balance of flesh, fat and bone, make sure, with the best advice obtainable, that your present condition is not the best for you. What is "normal" for the woman next door might become a flesh burden to you. And what is normal for you might soon send her to the land of no returning. Overweight and underweight bring two distinct sets of danger signals and lead to two equally unpleasant and unsafe destinations.—The Delineator.

The family physician of the future must have proportionate representation in the councils of his profession. No specialty or combination of specialties, not even general surgery, should be permitted to dominate the health affairs of a community or of a nation.—Wendell C. Phillips, J. A. M. A.